

Notice of Allowability

Application No.

09/518,297

Applicant(s)

LIM ET AL.

Examiner

Chih-Min Kam

Art Unit

1656

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 6/30/06.
2. ☒ The allowed claim(s) is/are 52,53 and 60-63.
3. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some* c) ☐ None of the:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. ☐ CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
- (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
- 1) ☐ hereto or 2) ☐ to Paper No./Mail Date _____.
- (b) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.
- Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

- | | |
|--|---|
| 1. <input type="checkbox"/> Notice of References Cited (PTO-892) | 5. <input type="checkbox"/> Notice of Informal Patent Application |
| 2. <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 6. <input type="checkbox"/> Interview Summary (PTO-413),
Paper No./Mail Date _____ |
| 3. <input type="checkbox"/> Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date _____ | 7. <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 4. <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit
of Biological Material | 8. <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9. <input type="checkbox"/> Other _____ |

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DETAILED ACTION

Status of the Claims

1. Claims 52, 53 and 60-63 are pending.

Applicants' amendment filed June 30, 2006 is acknowledged. Applicants' response has been fully considered. Claims 60-63 have been amended. Therefore, claims 52, 53 and 60-63 are examined.

Withdrawn Objection to New Matter Added to Specification

2. The previous objection to the specification, regarding new matters, is withdrawn in view of applicants' amendment to the specification in the amendment filed June 30, 2006.

Withdrawn Claim Rejections - 35 USC § 102

3. The previous rejection of claims 60-63 under 35 U.S.C. 102(b) as being anticipated by Bujard *et al.* (WO 94/29442) is withdrawn in view of applicants' amendment to the claims in the amendment filed June 30, 2006.

Examiner's Amendment

An **Examiner's Amendment** to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Brian Boyer on September 11, 2006.

Amendments to the Specification:

Please replace the description for SEQ ID NO:8 in Sequence Listing Table at page 3 of the amendment filed June 30, 2006 with the following term:

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VP16: aa 413-489 of herpes simplex virus viron protein 16 (no sequence shown)

Please cross out "8" for SEQ ID NO:8 in Sequence Listing Table at page 3 of the amendment filed June 30, 2006.

Please replace the description for SEQ ID NO:9 in Sequence Listing Table at page 3 of the amendment filed June 30, 2006 with the following term:

VP64: tetramer of aa 437-447 of ~~VP16~~ herpes simplex virus viron protein 16 (no sequence shown)

Please cross out "9" for SEQ ID NO:9 in Sequence Listing Table at page 3 of the amendment filed June 30, 2006.

Amendments to the Claims:

Claims 52 and 60-63 have been amended as follows:

52 (Currently amended) A method of producing a cell having a molecular switch for modulating gene expression, said method comprising:

(i) transforming said cell with a nucleic acid construct, having a DNA response element which binds a transcriptional regulatory protein, operably linked to a first promoter, a non-native compound-binding sequence which is the same as, overlapping, or adjacent to said DNA response element for binding to a DNA binding compound, and a transgene under the control of said first promoter, wherein the DNA binding compound is separate and different from the transcriptional regulatory protein; and

(ii) exposing said transformed cell to a DNA binding compound, wherein binding of the DNA binding compound to said compound binding sequence is effective to inhibit binding of a transcriptional regulatory protein to the DNA response element, thereby depressing or deactivating expression of the gene, where the transcriptional regulatory protein is a repressor or activator protein, respectively.

60. (Currently amended) A molecular switch, comprising:

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- (a) a first nucleic acid construct, having
 - (i) a DNA response element for a transcriptional regulatory protein, operably linked to a first promoter;
 - (ii) a non-native compound binding sequence which is the same as, overlapping, or adjacent to said DNA response element, for binding to a DNA binding compound;
 - (iii) a transgene under the control of said first promoter; and
 - (b) a DNA binding compound, wherein the DNA binding compound is separate and different from the transcriptional regulatory protein; and
 - (c) a second nucleic acid construct, having the coding sequence for said transcriptional regulatory protein operably linked to a second promoter;
- wherein said DNA binding compound, when bound to said binding sequence, is effective to modulate binding of said transcriptional regulatory protein to said DNA response element and wherein a first vector is including said first nucleic acid construct and a second vector is including said second nucleic acid construct.

61. (Currently amended) A molecular switch, comprising:
- (a) a first nucleic acid construct, having
 - (i) a DNA response element for a transcriptional regulatory protein, operably linked to a first promoter;
 - (ii) a non-native compound binding sequence which is the same as, overlapping, or adjacent to said DNA response element, for binding to a DNA binding compound;
 - (iii) a transgene under the control of said first promoter; and
 - (b) a DNA binding compound, wherein the DNA binding compound is separate and different from the transcriptional regulatory protein;
- wherein said DNA binding compound, when bound to said binding sequence, is effective to modulate binding of said transcriptional regulatory protein to said DNA response element and wherein said compound binding sequence has from about 8 to 20 nucleotides.

62. (Currently amended) A molecular switch, comprising:
- (a) a first nucleic acid construct, having

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(i) a DNA response element for a transcriptional regulatory protein, operably linked to a first promoter;

(ii) a non-native compound binding sequence which is the same as, overlapping, or adjacent to said DNA response element, for binding to a DNA binding compound;

(iii) a transgene under the control of said first promoter; and

(b) a DNA binding compound, wherein the DNA binding compound is separate and different from the transcriptional regulatory protein;

wherein said DNA binding compound, when bound to said binding sequence, is effective to modulate binding of said transcriptional regulatory protein to said DNA response element and wherein said nucleic acid construct has from 1 to 12 compound binding sequences.

63. (Currently amended) A molecular switch, comprising:

(a) a first nucleic acid construct, having

(i) a DNA response element for a transcriptional regulatory protein, operably linked to a first promoter;

(ii) a non-native compound binding sequence which is the same as, overlapping, or adjacent to said DNA response element, for binding to a DNA binding compound;

(iii) a transgene under the control of said first promoter; and

(b) a DNA binding compound, wherein the DNA binding compound is separate and different from the transcriptional regulatory protein;

wherein said DNA binding compound, when bound to said binding sequence, is effective to modulate binding of said transcriptional regulatory protein to said DNA response element and wherein said nucleic acid construct has from 1 to 12 tandem repeated transcriptional regulatory protein DNA response elements.

The following is an **Examiner's Statement of Reasons for Allowance**: The following references appear to be the closest art to the claimed invention. Goldstein *et al.* (U. S. Patent 5,527,690) teach sterol regulatory element (SRE) binding proteins (SREBP) are involved in the regulation of genes in cholesterol metabolism that is under the control of SRE-1, where SREBP-1, which acts not only as a transcriptional regulatory protein, but also as a DNA binding compound, binds to SRE-1 DNA sequences to promote transcription and gene expression; and Bujard *et al.* (WO 94/29442) teach a system for regulating expression of eukaryotic genes using

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components of the Tet repressor/operator/inducer system of prokaryotes in a host cell, and transcription of a nucleotide sequence operably linked to at least one tet operator sequence is stimulated by a tetracycline (Tc)-controllable transcriptional activator fusion protein (tTA), where the tTA acts not only as a transcriptional regulatory protein, but also as a DNA binding compound. However, the references do not teach or suggest a molecular switch comprising a DNA response element for a transcriptional regulatory protein, operably linked to a first promoter, a non-native compound binding sequence for binding to a DNA binding compound, a transgene under the control of said first promoter, and a DNA binding compound, wherein the DNA binding compound, which is separate and different from the transcriptional regulatory protein, and when bound to the binding sequence, is effective to modulate binding of the transcriptional regulatory protein to the DNA response element. Therefore, the claims are allowable over the art of record.


Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Primary Patent Examiner

 primary **CHIH-MIN KAM
PATENT EXAMINER**

CMK

September 11, 2006